Optimization Procedure for Hot Melt Extrusion as a Continuous Manufacturing Technique for Amorphous Solid Dispersions

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Introduction

Bulk & material properties
- Bulk density
- Powder flow
- Glass transition temperature

Figure 1. PVPVA Powder.

Extruder

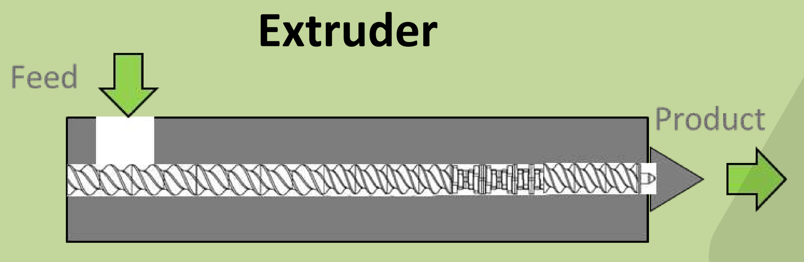
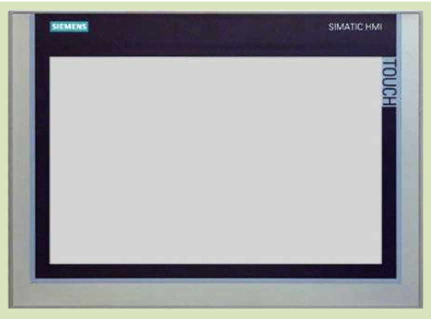


Figure 2. Hot melt extrusion.

Depending Critical Process Parameter
- Material temperature
- Pressure
- Specific feed load

Figure 3. Extrudate strand.

Critical Process Parameter



Process conditions
- Rotational speed
- Mass flow rate
- Barrel temperature

Extruder setup
- Barrel configuration
- Screw configuration
- Die geometry

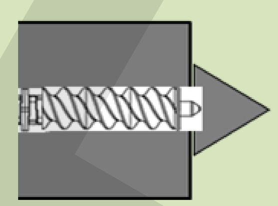


Figure 4. Extruder control panel [1].

Figure 5. Barrel, screw, die.

This work shall provide insights into the optimal selection of an operating point. Therefore, a two-step optimization procedure (Scale Independent Optimization Strategy, SIOS [2]) was applied for different polymers from pharmaceutical research. Additionally, a upstream granulation step was applied for one polymer to investigate the influence of the bulk properties of the polymers.

Materials and Methods

Extrusion
- K-Tron K-ML-SFS-KT20
- Leistritz ZSE 27 MAXX
- IR-Camera Testo 875

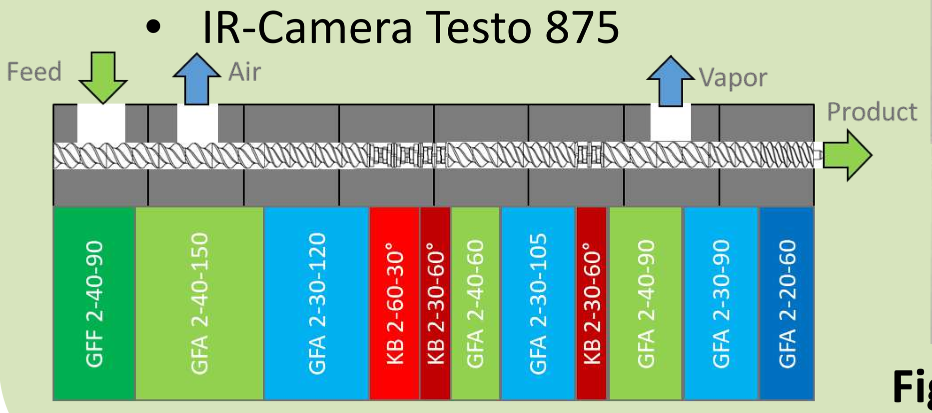


Figure 6. Screw and barrel configuration.

Figure 7. Experimental setup.

Material
- Soluplus, SOL (BASF, Ludwigshafen, Germany)
- Copovidone, PVPVA (Plasdone S-630, Ashland, Schaffhausen, Switzerland)
- Eudragit EPO, aPBMA (Evonik, Darmstadt, Germany)
- Granulated Copovidone, granPVPVA

Scale independent optimization scheme (SIOS)

1. Starting point
1 → 2 Increase of SFL by decrease of screw speed
2. Upper limitation of the operating window is exceeded → Backlog
2 → 3 Screw speed set to previous value
3. Optimal SFL is reached and autogenic extrusion started
3 → 4 Increase of screw speed and mass flow rate simultaneously
4. Optimized operating point

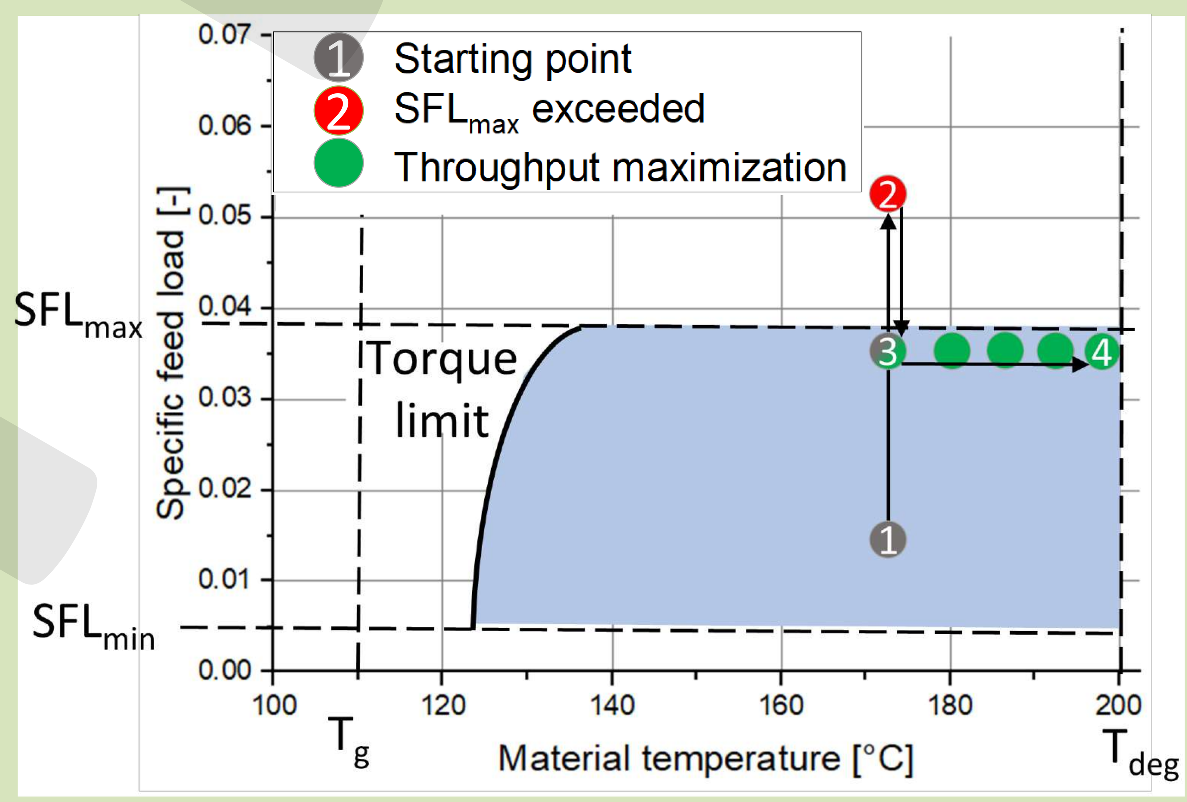


Figure 8. Schematic SIOS with exemplarily values.

$$SFL = \frac{\dot{m}}{d^3 \cdot n \cdot \rho}$$ (Mass flow rate $\dot{m}$, rotational speed n, screw diameter d, density ρ.)

Results and Discussion

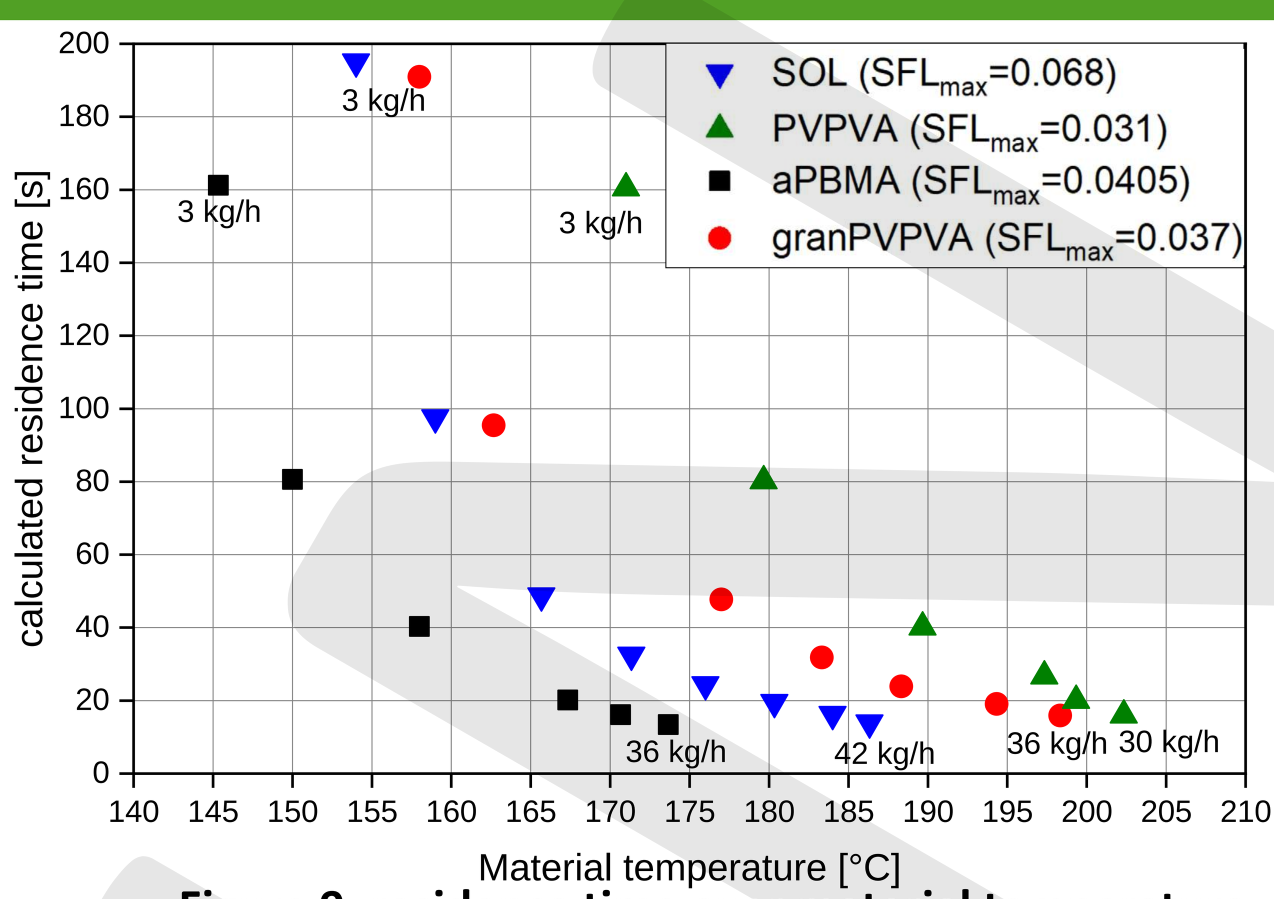


Figure 9. residence time over material temperature.

Similarities
- SIOS (including autogenic extrusion) suitable for all polymers
- Temperature decrease when autogenic extrusion is started
- No visible degradation at any point
- Final limitation caused by the dosing device

Table 1. Bulk properties and results of the SIOS for the different polymers.

Substance	*Bulk density [g ml⁻¹]*	*Tap density [g ml⁻¹]*	*Flowability [-]*	*SFL_{max} [-]*	*$\dot{m}_{max}$ [kg h⁻¹]*
SOL	*0.597*	*0.656*	*Excellent*	*0.0681*	*42*
PVPVA	*0.315*	*0.409*	*Passable*	*0.0309*	*30*
aPBMA	*0.339*	*0.418*	*Fair*	*0.0405*	*36*
granPVPVA	*0.451*	*0.575*	*Passable*	*0.0371*	*36*

Differences
- SFL_{max} → low bulk density and flowability leads to low SFL_{max}
- Temperature at similar conditions → Autogenic extrusion is leading to different viscosities
- $\dot{m}_{max}$ → low bulk density and flowability leads to low maximal mass flow rates
- Granulation step can improve SFL_{max} and maximal mass flow rate

CONCLUSION

In the present work it was shown that the selection of polymer for a HME has major influence on the process and the optimized operating point. Especially the bulk properties of the polymers should be kept in mind. Otherwise, an additional granulating step is a suitable upstream process for a maximized loading and throughput.

References: [1] https://www.leistritz.com (status: Jan. 22nd 2020)
[2] Wesholowski, J., et al.. Scale-Up of pharmaceutical Hot-Melt-Extrusion: Process optimization and transfer. Eur. J. Pharm. Biopharm. 2019

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